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EXAMINER	
KASTEN, ROBERT J	

ART UNIT	PAPER NUMBER
1795	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/533,015	Applicant(s) YANO ET AL.	
	Examiner ROBERT KASTEN	Art Unit 1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _28 April 2005_.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1-10_ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _1-10_ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _28 April 2005_ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _01/30/2006, 07/02/2008_.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is the first non-final action on the merits.

Claims 1-10 are rejected.

Drawings

1. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the copies of the drawings are substantially illegible for the purpose of providing structural insight into the applicant's invention. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear from the claims, as well as the

specification, how the separation medium is to be replaced in the intervening cavity by the connection medium. This limitation is found in claims 1, 6, 8 and 10. Claims 2-4, 7 and 9 are rejected as being dependant, either directly or indirectly, on claims 1, 6, 8 and 10.

Further concerning Claim 1, the claim language “and/or” renders the scope of the claim unclear, as the claim as written could require that both “the substance provided in the fluid substance be necessarily transferred with the fluid substance,” as well as “the substance provided in the fluid substance be transferred in the alternative to the fluid substance.” Claims 2-5 are rejected for being dependent, either directly or indirectly, upon an indefinite claim.

Further concerning Claims 5 and 9, the claims teach the limitation that the second cavity branches from the first cavity. However, according to claim 1 and the specification, the first cavity and the second cavity are joined by an intermediate cavity. It is unclear what structure or arrangement of cavities is being claimed, since the intersection of the first and second cavities could eliminate the intermediate cavity, which then renders the location of the separation and later controlling media also indefinite.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over LEE et. al. (US 2002/0170825), from here on referred to as LEE, in view of HOCHSTRASSER et. al. (US 4,874,490), from here on referred to as HOCHSTRASSER.

Concerning Claim 1, LEE teaches a method for two-dimensional electrophoresis on a microfluidics device. Specifically, LEE's invention is best exemplified with reference to Figure 6. Figure 6 shows a microfluidic device, specifically one with a grid

of microchannels or cavities: parallel cavities like 4 and 11 as well as orthogonal cavities 3 which make up a grid of first and second cavities.

a) As taught in [0038], a carrier ampholyte solution (the fluid substance) is added to one of the cavities and manipulated along the cavity using an array of electrodes which generate an electric field, resulting in electroosmotic flow of the fluid. The fluid is first subjected to an isoelectric focusing manipulation in the first dimension cavities [0041], and then can be transferred to the second dimension cavities [0011].

b) Initially, one set of cavities contain 0 voltage drop across them [0031], essentially limiting the movement of fluids between the two. When transfer of the fluid to the second medium is desired, however, the electric potentials between the electrodes may be brought from 0 to a set value, allowing flow out of the first dimension and into the second dimension, orthogonal to the first dimension [0011].

c) Thus, through the application of electric potential, the sample can be transferred from one dimension to the other.

LEE does not teach an intermediate cavity per se and further does not teach the need to replace a separation medium with a connection medium.

However, HOCHSTRASSER teaches a system for two-dimensional gel electrophoresis, utilizing two gels separated by an insulating (intermediate) layer that can be solid, liquid, or gas (col. 2, lines 22-39). The invention is best exemplified by figure 3, which shows a strip gel 26 and a slab gel 23 which are separated by a space 42 which is occupied by air. The first dimension of separation is permitted to occur on the strip gel with the air present in space 42. Once the desired amount of separation is

achieved in the first dimension, the two gels are placed in electrical contact for transfer from one gel to the other (col. 5, lines 3-24). One method of connecting the two gels is through the introduction of a new intervening gel between the first and second dimension gels (col. 5, lines 31-33).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to utilize the provided cavities of LEE to perform two-dimensional electrophoresis with an intermediate insulating space like in HOCHSTRASSER because the idea of performing two dimensional separation with insulating barriers to prevent transfer from one dimension to another is already known in the art and comprises the advantages of lessening the risk of zone distortion, as well as the incidences of inaccuracies and systematic error, by eliminating the need to transport a sample separated in a first dimension from one apparatus to another (HOCHSTRASSER, col. 2, lines 37-39). Structurally, the device of LEE contains all the components to perform the claimed method. However, LEE does not use an intermediate cavity to transfer sample from a first separation medium to a second separation medium or a separation medium to prevent such transfer. HOCHSTRASSER teaches the proper flow of sample (i.e. from one medium through an intervening space to a second medium), but does so without the array of cavities. In view of HOCHSTRASSER, it would have been obvious to use the device of LEE in a similar way because that new use required no structural changes and ultimately performed the same function, simply in a different direction. By way of example, one of ordinary skill in the art would have found it obvious to perform the following method on LEE's device: inserting a sample into cavity 11 of figure 3,

separating it until reaching intervening cavity 3, having the sample enter cavity 3, and having the sample enter into the second separating medium in cavity 4.

Concerning Claim 2, LEE in view of HOCHSTRASSER teaches all the limitations of claim 1. Further, LEE teaches that the device is for two-dimensional separations of proteins (abstract).

Concerning Claim 3, LEE in view of HOCHSTRASSER teaches all the limitations of Claim 2. Further, LEE teaches that the device may be used for two-dimensional electrophoresis [0027].

Concerning Claim 4, LEE in view of HOCHSTRASSER teaches all the limitations of claim 1. Further, LEE teaches in [0034] that the cavities may have a circular (tubular) cross-section. Finally, LEE teaches that the medium of the first separation dimension can be a carrier ampholyte solution [0038].

LEE does not expressly teach that the separation medium be a gas, nor does LEE specify whether the collection medium can be a liquid.

However, HOCHSTRASSER teaches that the separation medium can be a gas (col. 2, lines 30-31). Further, once the desired amount of separation is achieved in the first dimension, the two gels are placed in electrical contact for transfer from one gel to the other (col. 5, lines 3-24).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use gas as a separation medium in the modified device of LEE from claim 1 because gas has been shown as an effective method of preventing migration of species across regions in two-dimensional electrophoresis. Further, it

would have been obvious to use a liquid as the collecting medium in the modified invention of LEE in view of HOCHSTRASSER because the continuity between the liquid of the first separation dimension and the collection medium would make transport of the sample between the two much easier. Additionally, liquid would allow for an electrical connection between the first and second gel dimensions as in HOCHSTRASSER.

Concerning claim 5, LEE in view of HOCHSTRASSER teaches all the limitations of claim 4. Further, Figure 3 of LEE shows how an array of cavities branch from each other. At least one second cavity branches from at least one first cavity.

Concerning Claim 6, LEE teaches a device for two-dimensional electrophoresis on a microfluidics device. Specifically, LEE's invention is best exemplified with reference to Figure 6. Figure 6 shows a microfluidic device, specifically one with a grid of microchannels or cavities:

a) parallel cavities like 4 and 11 and,

b) orthogonal cavities 3 which make up a grid of first and second cavities.

c) As taught in [0038], a carrier ampholyte solution (the fluid substance) is added to one of the cavities and manipulated along the cavity using an array of electrodes which generate an electric field, resulting in electroosmotic flow of the fluid. The fluid is first subjected to an isoelectric focusing manipulation in the first dimension cavities [0041], and then can be transferred to the second dimension cavities [0011]. Initially, one set of cavities contain 0 voltage drop across them [0031], essentially limiting the movement of fluids between the two dimensions. When transfer of the fluid to the second medium is desired, however, the electric potentials between the electrodes may

be brought from 0 to a set value, allowing flow out of the first dimension and into the second dimension, orthogonal to the first dimension [0011]. Thus, through the application of electric potential, the sample can be transferred from one dimension to the other.

LEE does not teach an intermediate cavity per se, nor does LEE teach a cavity which separates first and second cavities.

However, HOCHSTRASSER teaches a system for two-dimensional gel electrophoresis, utilizing two gels separated by an insulating (intermediate) layer that can be solid, liquid, or gas (col. 2, lines 22-39). The invention is best exemplified by figure 3, which shows a strip gel 26 and a slab gel 23 which are separated by a space 42 which is occupied by air. The first dimension of separation is permitted to occur on the strip gel with the air present in space 42. Once the desired amount of separation is achieved in the first dimension, the two gels are placed in electrical contact for transfer from one gel to the other (col. 5, lines 3-24). One method of connecting the two gels is through the introduction of a new intervening gel between the first and second dimension gels (col. 5, lines 31-33).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to utilize the provided cavities of LEE to perform two-dimensional electrophoresis with an intermediate insulating space like in HOCHSTRASSER because the idea of performing two dimensional separation with insulating barriers to prevent transfer from one dimension to another is already known in the art. Structurally, the device of LEE contains all the components to perform the claimed method. However,

LEE does not use an intermediate cavity to transfer sample from a first separation medium to a second separation medium or a separation medium to prevent such transfer. HOCHSTRASSER teaches the proper flow of sample (i.e. from one medium through an intervening space to a second medium), but does so without the array of cavities. In view of HOCHSTRASSER, it would have been obvious to use the device of LEE in a similar way because that new use required no structural changes and ultimately performed the same function, simply in a different direction. By way of example, one of ordinary skill in the art would have found it obvious to perform the following method on LEE's device: inserting a sample into cavity 11 of figure 3, separating it until reaching intervening cavity 3, having the sample enter cavity 3, and having the sample enter into the second separating medium in cavity 4.

Concerning Claim 7, LEE in view of HOCHSTRASSER teaches all the limitations of claim 6. Further, LEE teaches that the device is for two-dimensional separations of proteins (abstract).

Concerning Claim 8, LEE teaches a device for two-dimensional electrophoresis on a microfluidics device. Specifically, LEE's invention is best exemplified with reference to Figure 6. Figure 6 shows a microfluidic device, specifically one with a grid of microchannels or cavities:

a) parallel cavities like 4 and 11 and,

b) orthogonal cavities 3 which make up a grid of first and second cavities.

c) As taught in [0038], a carrier ampholyte solution (the fluid substance) is added to one of the cavities and manipulated along the cavity using an array of electrodes

which generate an electric field, resulting in electroosmotic flow of the fluid. The fluid is first subjected to an isoelectric focusing manipulation in the first dimension cavities [0041], and then can be transferred to the second dimension cavities [0011]. Initially, one set of cavities contain 0 voltage drop across them [0031], essentially limiting the movement of fluids between the two dimensions. When transfer of the fluid to the second medium is desired, however, the electric potentials between the electrodes may be brought from 0 to a set value, allowing flow out of the first dimension and into the second dimension, orthogonal to the first dimension [0011]. Thus, through the application of electric potential, the sample can be transferred from one dimension to the other.

LEE does not teach an intermediate cavity per se, nor does LEE teach a cavity which separates first and second cavities.

However, HOCHSTRASSER teaches a system for two-dimensional gel electrophoresis, utilizing two gels separated by an insulating (intermediate) layer that can be solid, liquid, or gas (col. 2, lines 22-39). The invention is best exemplified by figure 3, which shows a strip gel 26 and a slab gel 23 which are separated by a space 42 which is occupied by air. The first dimension of separation is permitted to occur on the strip gel with the air present in space 42. Once the desired amount of separation is achieved in the first dimension, the two gels are placed in electrical contact for transfer from one gel to the other (col. 5, lines 3-24). One method of connecting the two gels is through the introduction of a new intervening gel between the first and second dimension gels (col. 5, lines 31-33).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to utilize the provided cavities of LEE to perform two-dimensional electrophoresis with an intermediate insulating space like in HOCHSTRASSER because the idea of performing two dimensional separation with insulating barriers to prevent transfer from one dimension to another is already known in the art. Structurally, the device of LEE contains all the components to perform the claimed method. However, LEE does not use an intermediate cavity to transfer sample from a first separation medium to a second separation medium or a separation medium to prevent such transfer. HOCHSTRASSER teaches the proper flow of sample (i.e. from one medium through an intervening space to a second medium), but does so without the array of cavities. In view of HOCHSTRASSER, it would have been obvious to use the device of LEE in a similar way because that new use required no structural changes and ultimately performed the same function, simply in a different direction. By way of example, one of ordinary skill in the art would have found it obvious to perform the following method on LEE's device: inserting a sample into cavity 11 of figure 3, separating it until reaching intervening cavity 3, having the sample enter cavity 3, and having the sample enter into the second separating medium in cavity 4.

Concerning claim 9, LEE in view of HOCHSTRASSER teaches all the limitations of claim 9. Further, Figure 3 of LEE shows how an array of cavities branch from each other. At least one second cavity branches from at least one first cavity.

Concerning Claim 10, LEE teaches a method for two-dimensional electrophoresis on a microfluidics device. Specifically, LEE's invention is best exemplified with reference to Figure 6.

a.) Figure 6 shows a microfluidic device as in claim 8, specifically one with a grid of cavities: parallel cavities like 4 and 11 as well as orthoganal cavities 3 which make up a grid of first and second cavities. As taught in [0038], carrier ampholyte solution (the fluid substance) is added to one of the cavities and manipulated along the cavity using an array of electrodes which generate an electric field, resulting in electroosmotic flow of the fluid. The fluid is first subjected to an isoelectric focusing manipulation in the first dimension cavities [0041], and then can be transferred to the second dimension cavities [0011].

b) Initially, the intermediate cavities contain 0 voltage drop across them, [0031] essentially limiting the movement of fluids between the two dimensions. When transfer of the fluid to the second medium is desired, however the electric potentials between the electrodes may be brought from 0 to a set value, allowing flow out of the first dimension and into the second dimension, orthogonal to the first [0011]. Thus, through the application of electricity, the uncharged separation medium is replaced with a charged connection medium. Electrophoresis is then be performed in a second dimension in a second cavity.

LEE does not teach an intermediate cavity per se, nor does LEE teach a cavity which separates first and second cavities.

However, HOCHSTRASSER teaches a system for two-dimensional gel electrophoresis, utilizing two gels separated by an insulating (intermediate) layer that can be solid, liquid, or gas (col. 2, lines 22-39). The invention is best exemplified by figure 3, which shows a strip gel 26 and a slab gel 23 which are separated by a space 42 which is occupied by air. The first dimension of separation is permitted to occur on the strip gel with the air present in space 42. Once the desired amount of separation is achieved in the first dimension, the two gels are placed in electrical contact for transfer from one gel to the other (col. 5, lines 3-24). One method of connecting the two gels is through the introduction of a new intervening gel between the first and second dimension gels (col. 5, lines 31-33).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to utilize the provided cavities of LEE to perform two-dimensional electrophoresis with an intermediate insulating space like in HOCHSTRASSER because the idea of performing two dimensional separation with insulating barriers to prevent transfer from one dimension to another is already known in the art. Structurally, the device of LEE contains all the components to perform the claimed method. However, LEE does not use an intermediate cavity to transfer sample from a first separation medium to a second separation medium or a separation medium to prevent such transfer. HOCHSTRASSER teaches the proper flow of sample (i.e. from one medium through an intervening space to a second medium), but does so without the array of cavities. In view of HOCHSTRASSER, it would have been obvious to use the device of LEE in a similar way because that new use required no structural changes and

ultimately performed the same function, simply in a different direction. By way of example, one of ordinary skill in the art would have found it obvious to perform the following method on LEE's device: inserting a sample into cavity 11 of figure 3, separating it until reaching intervening cavity 3, having the sample enter cavity 3, and having the sample enter into the second separating medium in cavity 4.

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number is (571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Sines can be reached on 571-272-1263. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/R. K./
Examiner, Art Unit 1795

/Brian J. Sines/
Supervisory Patent Examiner, Art Unit 1795